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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,634	10/11/2005	Brian Seed	00786/432002	4930

21559 7590 09/17/2007  
CLARK & ELBING LLP  
101 FEDERAL STREET  
BOSTON, MA 02110

EXAMINER
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WILSON, MICHAEL C

ART UNIT	PAPER NUMBER
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1632

NOTIFICATION DATE	DELIVERY MODE
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09/17/2007

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

## Office Action Summary

**Application No.**

10/521,634

**Applicant(s)**

SEED ET AL.

**Examiner**

Michael C. Wilson

**Art Unit**

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 20 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 13-17 and 20-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12, 18 and 19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 8-16-07.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 30-39 have been canceled. Claims 1-29 remain pending.

Applicant's election with traverse of Group I, claims 1-12, 18 and 19, in the reply filed on 7-20-07 is acknowledged. The traversal is on the ground(s) that the method of Group II requires the method of Group I and the methods of Groups I and II are both classified together. This is not found persuasive because the burden required to search and examine both groups together would be undue.

The requirement is still deemed proper and is therefore made FINAL.

Claims 13-17 and 20-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7-20-07.

Claims 1-12, 18 and 19 are under consideration.

#### ***Information Disclosure Statement***

A copy of the initialed information disclosure statement is attached.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the metes and bounds of what applicants consider “substantial sequence identity” cannot be determined from the specification or the art at the time of filing. The specification does not define the phrase. Nor does the art at the time of filing. Accordingly, those of skill would not be able to determine when they were infringing on the claim.

Use of “cell(s)” in claim 1 is indefinite because it is not clear that the plural is being claimed and because it does not clearly refer back to the “one or more mammalian cells”.

Claim 2 is indefinite because it does not further limit the artificial chromosome or cassette of claim 1. Nor does it clearly set forth a step of making the artificial chromosome by culturing cells (e.g. yeast cells) comprising a YAC and introducing a plasmid comprising the cassette into the cells. Clarification is required.

Claim 4 is indefinite because it does not make sense. Linear DNA is not “introduced” if a circular vector is inserted. The claim does not clearly further limit claim 2 because claim 2 does not require introducing a circular vector comprising the cassette. Claim 4 does not clearly set forth the steps of introducing a circular vector comprising the cassette into the host cell (e.g. yeast) and cleaving the circular vector to produce linear DNA comprising the cassette.

Claim 9 is indefinite because “the integration of said cassette” lacks antecedent basis. Furthermore, claim 9 does not clearly set forth how the “nucleic acid of interest” relates to the cassette, genetic modification or homologous recombination referred to in claim 1.

Claim 11 is indefinite because it does not further limit claim 1 because the “reporter gene” in claim 11 does not further limit the “selectable marker” in claim 1. In addition, the step of integration is unclear because it does not clearly set forth the reporter gene is operably linked to a promoter endogenous to the mammalian cell after integration.

Claim 12 is indefinite because it does not further limit claim 1 because the “detectable protein” in claim 12 does not further limit the “selectable marker” in claim 1. In addition, the step of integration is unclear because it does not clearly set forth the gene encoding the detectable protein is operably linked to a gene endogenous to the mammalian cell after integration such that a fusion protein is obtained.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-12, 18 and 19 are rejected under 35 U.S.C. 102(a) as being anticipated by Wilson (Analytical Biochem., Sept. 15, 2001, Vol. 296, No. 2, pg 270-278).

Wilson transfected mouse ES cells with a yeast artificial chromosome (YAC) having a first and second region of homology with the IL-10R $\alpha$  or PPAR $\gamma$  genes, a selectable marker (neo) operably linked to the CMV promoter or to thymidine kinase (pg 273, col. 2, “ES Transfection” and “Overview of the Procedure”; pg 274, Fig. 1; pg 275, Fig. 2; pg 276, Fig. 3; pg 277, Fig. 4). ES cells in which homologous recombination

occurs are selected using a probe (pg 273, "Isolation of a Probe to Screen G418-Resistant ES Clones). Correctly targeted ES cells were obtained (pg 277, col. 2, "ES cell transfection"). The YAC was produced by culturing yeast cells comprising YAC, then transforming them with linear DNA of cassettes (paragraph bridging pg 271-272), which is equivalent to claims 2 and 3. Claim 4 is included because it does not further limit how the linear DNA is introduced as compared to claim 2 (see 112/2<sup>nd</sup>). In the PPAR $\gamma$  example, contiguous regions of exon 5 are deleted (paragraph bridging pg 276-277; pg 277, Fig. 4), which is equivalent to claims 5 and 6. In the IL-10R $\alpha$  example, two exons and an intervening intron are deleted (pg 275, col. 2, Examples, line 9), which is equivalent to 7 and 8. Southern blot analysis showed the genes were deleted, which inherently indicates the amount of functional protein was less than 25% as claimed as in claim 10. Fig. 2 shows the various selectable marker strategies, which are equivalent to claim 11 and 12. The ES cell clones were used to make germline-transmitting chimeras (pg 277, last sentence in the caption of Fig. 4), which is equivalent to claim 19 because the germline-transmitting chimeras inherently transmit the deletion to both somatic and germ cells.

### ***Conclusion***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Angrand (Nucleic Acids Res., 1999, Vol. 27, No. 17, e16, i-vi)

Copeland (Nature Reviews, Genetics, October 2001, Vol. 2, pg 769-779)

Heintz (Nature Reviews, Neurosci., Dec. 2001, Vol. 2, pg 861-870)

Art Unit: 1632

Murphy (J. Bacteriology, April 1998, Vol. 180, No. 8, pg 2063-2071)

Muyrers (Trends in Biochemical Sci., May 2001, Vol. 26, pg 325-331)

Testa (Nature Biotech., April 2003, Vol. 21, pg 443-447)

Tsuzuki (Nucleic Acids Res., 1998, Vol. 26, No. 4, pg 988-993)

Yang (Nature Biotech., Sept. 1997, Vol. 15, pg 859-865)

Yang (Nature Biotech., April 2003, Vol. 21, pg 447-451)

Yu (PNAS, May 23, 2000, Vol. 97, No. 11, pg 5978-5983)

Zhang (Nature Genetics, October 1998, Vol. 20, pg 123-128)

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

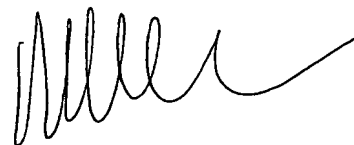
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Art Unit: 1632

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

A handwritten signature in black ink, appearing to read 'Michael C. Wilson', with a stylized, cursive script.

**MICHAEL WILSON**  
**PRIMARY EXAMINER**